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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/537,280

05/27/2005

Jane Sanders

AATH.P-001

1845

57381

7590

03/15/2011

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EXAMINER

WOODWARD, CHERIE MICHELLE

ART UNIT

PAPER NUMBER

1647

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/537,280	<b>Applicant(s)</b> SANDERS ET AL.	
	<b>Examiner</b> CHERIE M. WOODWARD	<b>Art Unit</b> 1647	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 January 2011.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 157-159, 162-171, 173-175, 179, 182-186, 189-192, and 195 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 121, 126, 127, 129, 130, 133-137, 198, 200-202, and 204-213 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Disposition of Claims: Claims pending in the application are 121,126,127,129,130,133-137,157-159,162-171,173-175,179,182-186, 189-195,198,200-202 and 204-213.

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## **DETAILED ACTION**

### **Formal Matters**

1. Claims 1-120, 122-125, 128, 131, 132, 138-156, 161, 172, 176-178, 180, 181, 187, 188, 193, 194, 196, 197, 199, and 203 have been cancelled by Applicant. Claims 157-159, 162-171, 173-175, 179, 182-192, and 195 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 121, 126, 127, 129, 130, 133-137, 198, 200-202, and 204-213 are under examination.

### **Response to Arguments**

#### **Claim Rejections/Objections Maintained**

2. The provisional rejection of claims 121, 126, 127, 129, 130, 133, 136, 137, and 198 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 63 and 65 of copending Application No. 12/333,714, is maintained for the reasons of record and the reasons set forth herein. Applicant's comments are noted, but the rejection is maintained.

3. Claim 121 and 198 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over at least claims 1-7, 10, and 13 of copending Application No. 12/527,218, for the reasons of record and the reasons set forth herein. Applicant's comments are noted, but the rejection is maintained.

#### **Claim Rejections - 35 USC § 102**

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 121 and 198 remain rejected under 35 U.S.C. 102(b) as being anticipated by Yoshida et al., (J Biol Chem. 1988;263(31):16341-16347) (cited on Applicant's IDS of 10/9/2009), for the reasons of record and the reasons set forth herein.

Applicant argues that Yoshida lacks an enabling disclosure of TRMo-2 and the specific monoclonal antibody does not appear to have been deposited with the ATCC nor is it characterized by

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sequence or in some manner that would allow a newly formed antibody to be identified as the same as TRMo-2.

Contrary to Applicant's arguments, Yoshida teaches how to make and use the TRMo-2 antibodies. The skilled artisan would reasonably know how to make and use the TRM—2 antibodies of Yoshida and test the same for activity. The requisite knowledge and skill in the art would not require undue experimentation to generate the TRMo-2 antibodies taught by Yoshida because Yoshida teaches how to make and use the TRMo-2 antibodies. As to Applicant's argument that the TRMo-2 antibody is not available at the ATCC, no evidence showing that an attempt was made either at the ATCC or the corresponding Japanese depository (given that Yoshida reference shows that Yoshida worked in the Department of Internal Medicine, School of Medicine, Keio University). Applicant is referred to MPEP 2405. See also:

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Applicant argues that, with respect to claim 198, no specific citation is provided as to the recited level of affinity within the Yoshida reference. Applicant argues that Yoshida does not provide a numeric affinity of TRMo-2 for TSH receptor. Applicant compares concentration levels of administration of the instantly claimed antibodies in instant Figure 1 with Figure 1 of Yoshida. Applicant argues that this comparison represents several orders of magnitude greater affinity for the receptor.

Applicant's arguments have been fully considered, but they are not persuasive. Comparative concentration levels upon administration to not necessarily correlate with receptor affinity. Applicant's comparative table is noted, but claim 198 only requires affinity for the TSH receptor of "at least  $10^{10} \text{M}^{-1}$ ". Absent evidence to the contrary, this limitation is met by the teachings of Yoshida.

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Applicant is reminded that claims 121 and 198 are drawn to a genus of monoclonal TSHR antibodies. Even if Applicant's antibody is not the same antibody as the TRMo-2 of Yoshida, the TRMo-2 antibody of Yoshida meets the limitations of the generic antibodies of the claims, as written. The examiner strongly recommends that Applicant further distinguish the instantly claimed antibodies from those of Yoshida. Reciting structural differences and other functional differences may be used to make this distinction.

6. Claims 126, 127, 129, 130, 133, 136, and 137 remain rejected in addition to claims 121 and 198 under 35 U.S.C. 102(b) as being anticipated by Yoshida et al., (J Biol Chem. 1988;263(31):16341-16347) (cited on Applicant's IDS of 10/9/2009), for the reasons of record and the reasons set forth herein.

Applicant incorporates the arguments set forth as recited above. Accordingly, the examiner responds as set forth above.

Applicant argues that in terms of inhibition, the instant TSHR1 hMAb is approximately 300x more potent than TRMo-2 and has a specific activity which is well outside the numeric ranges claimed. Applicant's arguments have been fully considered, but they are not persuasive. As Applicant has pointed out, inhibitory activity can be concentration dependent. The claims do not recite concentration limitations in terms of a comparative amount (units). Instead, they just recite "inhibitory activity." Stated another way, Applicant's arguments and Table 2 compare the concentration of MAb in terms of ng/ml. However, Yoshida makes the comparison in µg/ml. The units basis is important in the comparison because the units do not appear to be equivalent in Table 2 of Applicant's arguments and the unit concentration is silent in the claims. Similar issues are noted with regard to Table 3 of the remarks. Accordingly, absent evidence to the contrary, the TRMo-2 antibodies of Yoshida meet the inhibitory activity level of the claims in the absence of concentration limitations. Applicant is referred to Figure 1(b) (b) of Yoshida.

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Applicant is reminded that claims 121 and 198 are drawn to a genus of monoclonal TSHR antibodies. Even if Applicant's antibody is not the same antibody as the TRMo-2 of Yoshida, the TRMo-2 antibody of Yoshida meets the limitations of the generic antibodies of the claims, as written. The examiner strongly recommends that Applicant further distinguish the instantly claimed antibodies from those of Yoshida. Reciting structural differences and other functional differences may be used to make this distinction.

### **Claim Rejections - 35 USC § 103**

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 204-209, 212, and 213 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al., (J Biol Chem. 1988;263(31):16341-16347) (cited on Applicant's IDS of 10/9/2009), UniProt, Accession No. P16473 (sequence version 1, 1 August 1990) (previously cited of record), Zhong

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et al., (Yan Ke Xue Bao. 2002 Sep;18(3):185-9, Abstract), and Kohn et al., (J Clin Endo and Metab. 1997;82(12):3998-4009) (previously cited of record), as evidenced by WO 91/09137 (published 27 June 1991) (previously cited of record), for the reasons of record and the reasons set forth herein.

Applicant argues that the lack of enablement over Yoshida (as set forth and responded to above) is fatal to the instant obviousness rejection. As stated above, contrary to Applicant's arguments, Yoshida teaches how to make and use the TRMo-2 antibodies. The skilled artisan would reasonably know how to make and use the TRM—2 antibodies of Yoshida and test the same for activity. The requisite knowledge and skill in the art would not require undue experimentation to generate the TRMo-2 antibodies taught by Yoshida because Yoshida teaches how to make and use the TRMo-2 antibodies. As to Applicant's argument that the TRMo-2 antibody is not available at the ATCC, no evidence showing that an attempt was made either at the ATCC or the corresponding Japanese depository (given that Yoshida reference shows that Yoshida worked in the Department of Internal Medicine, School of Medicine, Keio University).

Applicant argues long-felt need as to the instant antibodies. Applicant's argument has been fully considered, but given the enabled teachings of Yoshida, a person of ordinary skill in the art at the time of the instant invention would have been able to make recombinant antibodies by using well-known methodologies and protocols, such as the ones taught by the Zhong et al., using the well-know sequence of the TSHR and the TRMo-2 human monoclonal antibodies taught by Yoshida, and the resulting structure and function of the recombinant antibodies would have been predictable. As stated of record, at the time of the instant invention, there were a finite number of identified predictable potential solutions recognized in the art to solve the problem making find human antibodies that can be practically and cost-effectively used as diagnostics and as immunotherapetueics for thyroid-based autoimmune disorders such as Graves' disease and Hashimoto's thyroiditis, as evidenced by WO 91/09137, p. 3, line 25-33, p. 4, lines 31-34, and p. 5, lines 26-34).

### **Claim Rejections - 35 USC § 112, First Paragraph**

#### **Written Description**

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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12. Claims 134, 135, 200-202, 210, and 211 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Applicant argues that the claims are directed to antibodies or fragments. Applicant argues that the specification states that the binding partner can have a VH domain without a VL domain. Applicant also argues that one or more CDRs can be incorporated to a suitable framework to confer the binding and stimulating properties of the recited antibody. Applicant also argues *Capon v. Escher*, 76 USPQ2d 1078 (Fed. Cir. 2005) and argues that constructing antibodies is routine in the art.

Applicant's arguments have been fully considered, but they are not persuasive. The specification does not provide an adequate description of the structure of the antibodies such that the skilled artisan would be aware that Applicant was in possession of the genera of claimed antibodies. Further, the specification does not adequately describe operative embodiments of the claims in their full scope

The instant claims are drawn to antibodies with only a partially defined structure. Screening procedures are known in the art to identify VL domains that can be combined with a VH domain to produce antibodies that bind the same epitope as the parent antibody. While the VH and VL CDRs can be sufficient structure to define an antibody that binds to the same antigen as the parent antigen, the instant claims encompass antibodies and fragment thereof whose structure has not been adequately defined. Neither the specification nor the art support a sufficient definition of antibody structure based on the partial structures recited in the instant claims, wherein the antibodies bind to epitopes different than the parent antibody from which the partial structures are derived. Thus, the specification does not provide a correlation between structure and function for the antibodies as broadly claimed. Neither the specification nor the art support a sufficient definition of antibody structure based on the partial structures recited in the instant claims, wherein the antibodies bind to epitopes different than the parent antibody from which the partial structures are derived. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

As stated of record, the instant claims recite antibodies with functional characteristics, but only limited partial structure. For example, claim 134 recites alternative structural embodiments where the VH domain may be SEQ ID NO: 1 or one or more VH CDRs from SEQ ID NO: 2, 3, or 4. No VL domain is recited in the claim and the limited alternative embodiments of the structure of the VH domains, which are, in the alternative, limited to only one CDR, do not adequately describe the structure of the claimed genus of antibodies. Claim 200, for example only describes a VH domain and no VL domain is disclosed. Claims 201 and 202 recite one or more VL or VH CDRs, but not both, and not all of the

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CDRs, including CDR3, which is known to be critical for binding, are disclosed. This results in an incomplete structural description of the claimed genus of antibodies and this structural insufficiency results in an inadequate description of starting material, such that one of ordinary skill in the art would be aware that Applicant was in possession of the claimed genus.

It is suggested that Applicant focus the claims on structures described in the specification and the prior art in order to overcome the instant rejection.

### **Conclusion**

NO CLAIM IS ALLOWED.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **CHERIE M. WOODWARD** whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:30am-6:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CHERIE M WOODWARD/  
Primary Examiner, Art Unit 1647